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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,498	07/07/2003	Alan P. Kozikowski	9328-051-999	8108

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EXAMINER

DESAI, RITA J

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 05/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/614,498

**Applicant(s)**

KOZIKOWSKI ET AL.

**Examiner**

Rita J. Desai

**Art Unit**

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-91 is/are pending in the application.
- 4a) Of the above claim(s) 9-31 and 33-91 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/03</u> . | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

Applicants have elected group II of the restriction claims 1-8 , 32 in part drawn to formula I wherein R1 is a aryl. The examiner has rejoined group I and III in part wherein R1 is a cycloalkyl.

Thus now the group includes R1 to be an aryl, cycloalkyl and a hetero cyclo.

If the compound claims are found to be allowable then the method of treating cancer claims 41, 51, 60, 61, 64, 73, 74, 75, 81, 90 and 91 limited to the scope of the elected group (formula I wherein R1 is an aryl, cycloalkyl or 3to 10 membered heterocycloalkyl).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R1 to be a phenyl and adamantly , does not reasonably provide enablement for any other cylcoalkyl or any 3-10 membered heterocylic group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or

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use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

**1) The breadth of the claims:** The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

**2) The nature of the invention:** The invention is a hydroxyamido compound that is useful to treating cancer.

**3) The state of the prior art:** The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group versus a hydrogen changes the properties altogether. A good example is a theophylline versus caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. Applicants R1 is drawn to hetero ring and cycloalkyl and also aryls. Hetero ring due to the presence of other atoms such as N, S and O have different electronegativity and hence bonding and properties. Thus they would not behave in the same way as an aryl. Also there is very little known in the treatment of cancer and the state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment of any and all cancers, as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

**4) The level of one of ordinary skill:** The ordinary artisan is highly skilled.

**5) The level of predictability in the art:** It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The level of unpredictability in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

**6) The amount of direction provided by the inventor:** The inventor provides very little direction in the instant specification. There are no examples with the R being heterocyclic groups and also there is no data provided to show that these compounds do indeed treat cancer or even have any histone deacetylase activity.

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**7) The existence of working examples:** The instant specification does not have any working examples nor any invitro or invivo data that they do have any activity.

**8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:** Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

“A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable.”

***Claim Rejections - 35 USC § 103***

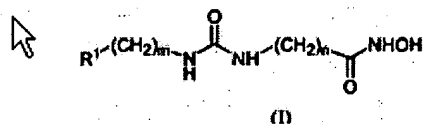
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Victoria Richon et al 1998 and also WO0226696 Watkins et al 2002.

Applicants claims are drawn to

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wherein R1 is an aryl, or a cycloalkyl or a heterocycloalkyl,

### **Determination of the scope and content of the prior art (MPEP §2141.01)**

The reference Richon et al teaches various compounds, see table 1 page 3004 . particularly compound 7 .

Also see the teaching on page 3005 that UCHA is the most potent HPC.

### **Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)**

The compound 7 of the prior art differs by just one CH2 linkage since applicants m is 1 to 10.

The reference teaches the structural similarity is the terminal hydromic group.

See the results section on page 3004.

WO0226696 Watkins et al 2002 on page 57 aryl and heteroaryl groups not directly linked. See compound 46, 48, 49 on page 57. These compounds are also HDAC inhibitors

### **Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)**

Thus with the prior art teaching that these similar compounds have an activity to inhibit histone deacetylases and also with the teaching of the various groups as given in the table 1 of the Richon reference and the compounds as given on page 57 of the WO'696 document , one would be motivated and would find it prima facie obvious to make a compound which was not directly linked to the NH-C(O)-NH to obtain the compounds of the invention.

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***Conclusion***

Claims 1-8 and 32 are rejected.

Claims 9-31, 33-91 are withdrawn since they are drawn to non elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, 9:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita J. Desai  
Primary Examiner  
Art Unit 1625

R.D.  
May 4, 2006

*RDesai*  
*5/4/06*